

Authenticity of Zinc Oxide Nanoparticles and Zinc Oxide Playing Vital Role in Wound Healing

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ABSTRACT

A wound is a break in the continuity of the skin. As the skin's continuity is disrupted, the body's internal organs are visible. This is a precarious condition that could result in death. The wound healing process begins with the skin's immediate reaction after a wound. The whole procedure starts by itself. This process can be aided in many ways, including keeping the wound clean of bacterial infection and moisture and dust. A variety of agents are added therapeutically to the wound site for this purpose. All of them are zinc oxide. It has a lot of wound-healing effects. It reduces the number of bacteria at the wound site, especially Staphylococcus aureus and Escherichia coli. All of these bacteria infiltrate the wound site and is a leading cause of wound healing delays, among many others. It is hypothesised that by converting zinc oxide into nanoparticles, wound healing efficacy would be enhanced. Because of their small scale, nanoparticles have greater penetration capacity.

Keywords: Honey, Zinc Oxide, nanoparticles, Wounds Healing.

INTRODUCTION

A wound is a trauma-induced injury, particularly one that affects an animal's skin and flesh. In surgery, the term wound refers to a solution of continuity or interruption of the soft part of the body due to external trauma, but in medical terms, it refers to an injury to any part of the body caused by an agent as a result of external trauma, regardless of

whether the surface is broken or not (Buffoni et al., 1993).

Iron is the most abundant element in the human body. In terms of a body's mineral profile, zinc comes in second. When the zinc content of the dermis and epidermis were compared, the epidermis had five to six times more zinc than the dermis. A lot of transcription factors contain zinc as a cofactor.

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It is a necessary component of metalloenzymes, which include zinc-dependent metalloproteinases matrix. All of these factors influence keratinocyte migration and wound auto-debridement. They also encourage wound remodelling (Roston et al., 2002; Agay et al., 2005; & Lansdown et al., 2007).

Many studies have been conducted to demonstrate the effectiveness of zinc in wound healing. Zinc-containing preparations have been shown to improve wound healing and control bacterial infection at the tissue site. They also aided in the formation of granulation tissue at the site of the wound (Ehrlich, 1998, & Rostan et al., 2002).

Antimicrobial nanoparticles, which were recently introduced, have proven to be extremely beneficial, particularly in wound healing. In addition to overcoming bacterial resistance, it has reduced acute toxicity. When compared to traditional antibiotics, it has also reduced the cost of treatment. Nanoparticles stay in the body for longer periods of time than other antibiotics, resulting in longer-lasting therapeutic effects (Jung et al., 2011).

After studies on their effect on wound healing, zinc oxide nanoparticles have become very popular. These studies have yielded promising outcomes. Zinc oxide nanoparticles have very unique antibacterial properties, preventing wound infection by inhibiting bacterial colonies of *Staphylococcus aureus* and *Escherichia coli* in wounds. Furthermore, zinc oxide nanoparticles promote wound healing (Rao et al., 2013).

Infection from a burn wound is a serious problem that both animals and humans must deal with. Because in this case, epidermal maturation is delayed, resulting in the formation of additional scars. Microorganisms infiltrate the tissue layer beneath the dermis, causing severe bacteremia and sepsis (Piotr et al., 2007).

According to a report, *Pseudomonas aeruginosa* or methicillin-resistant *Staphylococcus aureus* is responsible for 75% of mortality after burn wounds. Both are highly susceptible to zinc oxide

nanoparticles. As a result, zinc oxide nanoparticles can be used to treat burn wounds more effectively (Shokotihi et al., 2011).

Review of literature

Bang et al. (2007) investigated the effect of Zinc supplementation on burn wound healing. He stated that after a burn injury, the body's nutritional requirements significantly increase. Zinc levels were measured before and after a burn wound was inflicted on an animal model in this study. After a burn wound, the therapeutic effects of zinc were determined by measuring zinc levels in blood serum. They divided into four groups. There were twenty rabbits in each group. Each group had a different diet plan. The first group, designated A, was given a diet with a normal zinc concentration. The second group, designated B, was given a zinc-supplemented diet. The third group, designated C, was fed a diet that depleted zinc levels. The control group was the last group marked with a D. This group had no inflicted wounds and was given a diet plan with a normal zinc concentration. Before inflicting burn wounds on all animals, their serum profiles were evaluated, and they were continuously monitored until day 56 of the trial.

The copper and zinc ratios in the blood were measured. Zinc levels in group B were low before the burn wounds and remained low until the third week after the burn wound. However, at the fourth week, there was a significant increase in zinc levels ($p < 0.05$). Zinc levels were lower in group A after a burn wound was induced, and this pattern continued until the end of the study period. After burn induction, there was a significant decrease in zinc levels in group C ($p < 0.05$). The zinc levels in group D, which was used as a control group and had no wounds, remained unchanged. Copper concentrations were significantly higher in groups B and C ($p < 0.05$).

In the first four weeks, the value of copper in group A was very high. Following that, it began to decline. Zinc and copper levels were found to be inversely proportional until the fourth week. They were able to

recover after that. Photography was used to check the healing time and contraction rate. The animals in group B had the most wound contraction. In this group, healing time was also the shortest. Finally, it was determined that zinc plays an important role in wound healing. As a result, adding zinc to the diet of animals with burn wounds is beneficial.

Clayssen et al. (2010) conducted a study to see how zinc, when included in the diet, affected wound healing. They enlisted the help of two groups of rats for this project. The first group was designated as the control group, and they were fed a diet containing 80 parts per million zinc. The second group received a zinc deficiency dose of ten parts per million. Before inflicting burn wounds on rabbits, this diet plan was followed for ten weeks. Zinc is a good antioxidant with a positive effect on wound healing. Twenty percent of the rabbits' body area was burned after ten days of conditioning.

Animal blood samples were taken in order to perform a blood profile. From day one to day ten, blood samples were taken. The levels of plasma oxidative stress, zinc status, and antioxidant enzymes were all tested. When the data was analysed, it was discovered that stress markers increased and zinc levels decreased in group two before the burn wound was inflicted. Zinc levels increased in the liver after a burn injury, but decreased in the bone and plasma. Zinc depletion has no effect on oxidative stress in burn wounds, according to the findings. Further research into the effects of zinc supplementation on wound contraction and healing time is recommended, as it has already been shown to be beneficial.

Honey's wound healing efficacy was investigated by Jalali et al. (2007). Honey is said to have a significant effect on wound healing. Honey has also been reported to speed up the healing of burn wounds. Honey has a variety of properties that vary by region and depend on the flower from which honey bees collect nectar. Dogs were chosen as experimental units for this study. A total of ten healthy dogs were chosen. They were between the ages of four and five. Their weight ranged

from 15 to 25 kilogrammes. Wounds were inflicted on the animals' dorsolateral region. They were broken up into two groups. There were five dogs in each group. Honey was used as a topical treatment for Group A.

The wounds in Group B were treated with normal saline and were considered the control group. On a daily basis, wounds were observed and microbiological examinations were performed. It was completed on the first, seventh, fifteenth, and twenty-first days. In comparison to the control, the results supported the hypothesis that honey has remarkable wound healing efficacy. The time it took for a wound to heal was significantly reduced ($p < 0.05$). Microbiological tests revealed that wounds treated with honey had a lower bacterial count. As a result, it was determined that honey has a significant impact on burn wound healing, as it reduced wound healing time and bacterial count, keeping wounds free of exudate.

Zhang et al. (2007) conducted a study to see how effective zinc and insulin are at healing wounds. Insulin administration has been shown to have a positive effect on wound healing. When administered locally, insulin has a hypokaleamic effect. Rabbits were chosen as the test animals. Dermatome was used to inflict partial thickness skin wounds on rabbits' backsides. Insulin was injected first, followed by zinc injections at various concentrations at the wound site. Animals were divided into two groups after this procedure. There were seven rabbits in each group. The first group received a combination of zinc and insulin injections. The second group was given only zinc and was referred to as the control group. Both groups' wound parameters were investigated. The rate of wound contraction and healing time were investigated. Injections of insulin combined with zinc were found to hasten wound healing. The rate of wound contraction was also increased in this group. As a result, the researchers came to the conclusion that combining insulin and zinc speeds up wound healing.

The wound healing efficacy of watercress oil on burn wounds was investigated by Abu-Zinadah (2008). Rabbits were chosen as the experimental model. For this, they enlisted the help of 32 rabbits. They were split into eight groups, each with four rabbits. Burn wounds were induced in the first four groups using concentrated HCl, while burn injuries were induced in the last four groups using red hot glass rods at a temperature of 80 degrees Celsius. The treatment protocol was set up so that two groups received only normal saline treatment because they were designated as the control group. Bacitracin and Neomycin were used in a combination treatment for two other groups. The other two groups were given watercress oil and the remaining two were given watercress oil and *Nigella sativa* oil. Each group's four parameters were investigated. Wound contraction rate, wound epithelization, wound healing time, and granulation tissue formation were the variables studied.

The inflammatory cell response in the wound periphery was examined using histopathology. This process also determined hair follicle growth, repair, and thickness. Watercress was found to have antibacterial and anti-inflammatory properties. When the results were compared to those of the control group, it was discovered that those who were given watercress and antibiotics had better wound healing abilities. Their parameters, such as wound contraction rate and healing time, justified this. However, combining watercress and *Nigella Sativa* did not produce any positive results. Watercress oil was found to be beneficial in the healing of burn wounds at the conclusion of the study.

Yaman et al. (2010) conducted a study on burn wounds to compare the wound healing effects of collagenase and silver sulfadiazine. They inducted sixty rats for this purpose. These were all men. They were split into three groups, each with twenty rats. The backside of rats was chosen to create partial-thickness burn wounds. Collagenase was used to treat the first group. Silver sulfadiazine was used to treat group two. The third group was designated as

the control group. Cold cream was used to treat it. The treatment was carried out on a daily basis. It was continued until the patient recovered. A histopathological analysis was also performed. Tissue samples were taken on days ten and fourteen for this study. Wound healing time and wound contraction rate were the parameters to be assessed. Collagenase has a significant effect ($p < 0.0001$) on burn wound healing when compared to the control group, according to statistical analysis. As a result, it was determined that collagenase is an effective wound healer, particularly for burn wounds, and that it can be used to treat burn wounds.

Fuller et al. (2009) conducted research to confirm the negative effects of silver sulfadiazine use. Silver sulfadiazine was previously recommended for use in burn wounds. However, it has been reported to cause allergic reactions, hyperosmolality, hemolysis, and methemoglobinemia. However, this claim lacked credibility and was unsupported by evidence. This study's sole purpose was to look into this claim. The use of silver sulfadiazine has also been linked to leukopenia. After the study, it was determined that all of the claimed side effects are untrue, and that using silver sulfadiazine to treat burn wounds is completely safe. Other topical agents used in conjunction with silver sulfadiazine caused the reported side effects.

The effect of virgin fatty oil on burn wound healing was investigated by Djerrou et al. (2009). Six male rabbits were chosen for this purpose. On the backsides of the rabbits, four third-degree burn wounds were created. The first rabbit was used as a control group and received no treatment. The remaining rabbits were given a variety of treatments that are currently being studied. One wound was treated with virgin fatty oil at a concentration of 0.5 gm per 1 ml. Vaseline was used to treat the remaining wounds. This treatment was done every day until the healing was complete. The rate of wound contraction was measured, as well as the time it took for the wound to heal. At the end of the study, it was discovered that virgin fatty oil performed better than Vaseline and the control group treated with

normal saline in terms of wound healing. In wounds treated with virgin fatty oil, re-epithelization was also quick. Finally, the results of the study show that in wounds treated with virgin fatty oil, wound contraction rate increases significantly and epithelization time decreases noticeably. As a result, it is suggested that it be used to treat burn wounds.

Malik et al. (2010) conducted a study to compare and contrast the wound healing efficacies of two wound healing agents. Honey and silver sulfadiazine were the active ingredients. They were put to the test on animal models by inflicting burn wounds on them. Rabbit models were given partial thickness and superficial burn wounds. Silver sulfadiazine was applied topically to some animals, while honey was used to treat wounds on others. Some animals were also declared to be in control, and their wounds were simply washed with regular saline. Wound re-epithelization and healing time were two parameters that needed to be investigated in order to justify our findings. The drawn conclusion revealed to us that topical application of honey is superior in wound healing efficacy over silver sulfadiazine and the control group at the end of the study period.

Ghasem et al. (2010) looked into the effects of honey and zinc sulphate in combination. Honey, in combination with zinc sulphate, given either as a supplement or as a topical, was said to improve wound healing, according to their hypothesis. They conducted a study to demonstrate this. They chose rats for the experiment. Animals were given wounds, which were then treated with the agents under consideration. Some animals received only honey treatment, while others received only zinc sulphate topical application and dietary supplementation. One group received both topical honey and zinc sulphate application as well as zinc sulphate supplementation in the diet. Wound re-vascularization, collagen fibres, and wound re-epithelization were all investigated. Following the study, the results obtained from the aforementioned parameters revealed that

applying honey and zinc sulphate to wounds has a significant effect on wound healing. However, when both agents are used together, they have a synergistic effect and accelerate wound healing, which is far better than when they are used separately. As a result, their combination in wound healing is recommended.

The effect of topical application of zinc oxide on hypertrophic scars was investigated by Aksoy et al. (2010). These scars are self-proliferating. There has been no recent research on the prevention and treatment of proliferative scars. Furthermore, their aetiology and biology remained unknown. Rabbits were used as test subjects. Artificially induced hypertrophic scars on rabbit ears were studied. These scars were in the shape of a circle. For this experiment, a total of ten rabbits were enlisted. They were split into two groups, each with five rabbits. The first five rabbits were given a treatment of 40% zinc oxide ointment. The other five were designated as the control group, and their wounds were treated with a non-therapeutic ointment. The wounds were treated with zinc oxide for another twenty-one days. Those in the control group received a placebo treatment for 42 days. Specimens were taken from healed wound sites and sent to the laboratory for tensile strength and histopathological examination after the treatment protocol was completed. Each specimen was split into two halves, one for tensile strength and the other for histopathology. Scar hypertrophy decreased significantly ($p=0.017$) in wounds treated with zinc oxide ointment, according to histopathological examinations. Furthermore, those wounds treated with zinc oxide ointment had higher tensile strength. Histopathological examination revealed that nodule formation was reduced in wounds treated with zinc oxide ointment. As a result, the conclusion reached was in favour of the use of zinc oxide for the treatment of hypertrophic scars, as the findings of the previous study indicated that their use yielded promising results.

Yaman et al. (2010) compared the effects of silver sulfadiazine and cold cream

on wound healing efficacy. For this experiment, they chose fifty-four male rats. They were split into three different groups. On the backsides of the rats, burn wounds were inflicted. Group one was treated as a control group, and its wounds were simply washed with regular saline. Silver sulfadiazine was used to treat Group B. The final group was given cold cream as a standard treatment. The trial lasted fourteen days, with results recorded on days four, nine, and fourteen. Specimens were taken from the wound's healed zone and sent to a lab for histopathological analysis. When compared to control, histopathology of wounds revealed that both cold cream and silver sulfadiazine are effective at wound healing. Significant differences in results were found in all three groups ($p < 0.001$), according to statistical findings. As a result of the above experiment, it is now clear that silver sulfadiazine and cold cream can be used to treat burn wounds.

Dua et al. (2010) conducted a study to demonstrate norfloxacin's therapeutic effects on burn wound healing. Norfloxacin was used in transdermal plasters for this purpose. The researchers wanted to see if the above-mentioned drug had antimicrobial properties because microbial invasion is a common problem in burn wound healing. Polymers of two types, PVA and PVP, were used to make transdermal plasters. Norfloxacin was incorporated into polymers at various concentrations. Silver sulfadiazine was used as a comparison drug to norfloxacin. Wound contraction rate, healing time, tensile strength, and histopathological examinations were among the parameters to be studied. A microbiological test was also performed on a sample taken from the wound site. At the conclusion of the study, the findings revealed that norfloxacin is more effective than silver sulfadiazine in preventing bacterial invasion at the wound site and reducing healing time. The tensile strength of the tissue was also improved. As a result, norfloxacin is recommended for the treatment of burn wounds.

The effectiveness of silver dressing against methicillin-resistant *Staphylococcus*

aureus was investigated by Lee et al. (2010). When used for wound healing, silver dressings are thought to have superior antibacterial properties. A study involving 108 rats was conducted to demonstrate this. On the backside of each rabbit, wounds were inflicted. They were split into six different groups. Each group was given a unique treatment. The first group received a nanocrystalline silver dressing. The second group was given a cellulose dressing containing silver carboxy methyl. The third group was given silver sulfadiazine, which was sold under the brand name Medifoam silver. The fourth group received nanocrystalline silver dressing, but this belonged to a different trade group. The animals in group five were given a drug called "Ilvodon," which contained the active ingredient silver sulfadiazine. The wounds of Group 6 were treated with a ten percent concentration of povidone iodine as a control group. Histopathological examination, bacterial count, and wound contraction rate were the variables investigated. Wounds treated with nanocrystalline silver dressing had the fastest wound contraction rate. In wounds treated with nanocrystalline silver, the same was true in terms of granulation tissue formation and inflammatory cell proliferation. Microbiological tests revealed that wounds treated with nanocrystalline silver dressing had a high zone of inhibition. According to this study, silver-containing dressings are beneficial for wound healing because they inhibit bacterial proliferation at the wound site and improve wound healing. However, among all silver-containing dressings, nanocrystalline silver dressing outperformed all others in terms of reducing the population of methicillin-resistant *Staphylococcus aureus* at the wound site.

Al-Saeed (2011) conducted a study to see how effective zinc sulphate is at healing burn wounds. Rabbits were chosen as experimental animals for the desired purpose. On the backsides of the animals, burn wounds were inflicted. Chemical burns were the cause of these wounds. This was accomplished by using concentrated hydrochloric acid at a

concentration of 80%. There were a total of twelve rabbits chosen. They were split into two groups, each with six rabbits. The first group of animals were given zinc sulphate orally at a dose rate of 25 milligramme per kilogramme of body weight. The second group was given only normal saline. The experiment lasted twenty-one days. Hair growth and wound diameter were examined in order to justify the use of zinc sulphate. Daily observations were kept track of. After the study, it was discovered that zinc sulphate is beneficial for the healing of burn wounds because it reduces healing time and promotes hair growth.

A study by Bairy et al. (2011) compared the healing efficacy of sodium fusidate and framycetin sulphate on burn wound healing. Topical bacterial infection is frequently treated with sodium fusidate and framycetin sulphate. However, their use as a burn wound healer has never been documented. The primary goal of this study was to compare the effects of sodium fusidate and framycetin sulphate on wound healing. Rats were chosen as the experimental animals. On the backsides of rats, partial thickness skin wounds were induced. Metallic cylinders containing molten wax at a temperature of 80 degrees Celsius were used to inflict wounds. In the experiment, a total of seventy rabbits were used. They were split into seven different groups. They were anaesthetized prior to wound infliction to prevent pain tolerance. Group one served as the control group, with wounds treated with normal saline at the wound site. Fusidate was applied topically to the animals in group B. Sodium fusidate was given to the third group. Fusidic acid was used to treat group four. Framycetin A was applied topically to group five rats. Framycetin B was given to group six. Framycetin was used to treat Group 7. The drug was applied to the skin twice a day on a daily basis. Histopathological studies were conducted, as well as wound contraction rate and wound epithelization time. The study period was twenty-one days long. At the conclusion of the study, it was discovered that wounds treated with sodium

fusidate and framycetin A had a higher rate of wound contraction. The time it took for wounds in groups one and five to epithelize was also long. The histopathology of wounds was used to determine this. At the conclusion of the study, sodium fusidate and framycetin were found to be superior to all other treatments in terms of wound healing time and epithelization, and their results were statistically significant.

Al-Waili et al. (2011) conducted experiments to prove the efficacy of honey as a wound healer for burn wounds and ulcers. These types of wounds are common and a major problem all over the world. For the healing of these wounds, a variety of treatments have been proposed. One of them is honey. However, the goal of this research was to learn more about honey's mechanism of action and how it works as an antibacterial agent. Honey's action is revealed by a study conducted by a group of researchers. Honey acts as an antioxidant. It reduces the formation of scar tissue while also enhancing the epithelization process. Honey is an excellent agent to use at the wound site because of all of these properties. Honey helps to keep wounds free of bacterial contamination and speeds up wound healing. As a result, it is an effective treatment for burn wounds and ulcers.

Nagoba et al. (2011) conducted a study to confirm citric acid's wound healing efficacy, particularly in the treatment of chronic wounds. When it comes to wound care, chronic wounds present a significant challenge. They almost never respond to treatment. Infection spreads quickly in such wounds, and the animal may die as a result. Chronic wounds can be infected with a variety of infections, including viral, bacterial, and fungal infections. All of these factors contribute to chronic wound healing taking longer. There were a total of 38 cases chosen, all of which had chronic wounds. They didn't seem to respond to any treatment. All of the cases were split into two groups, each with nineteen animals. One group was given a three percent citric acid topical treatment. The other group received a 5% citric acid treatment.

After ten to twenty applications of 3 percent citric acid, the wounds of the first group healed. Before their wounds healed, the second group received seven to fifteen applications of 5% citric acid. The findings of this study supported citric acid's efficacy, particularly in the treatment of chronic wounds. Citric acid prevented bacterial, fungal, and viral contamination of the wound. The rate of wound healing and contraction was also improved. All of these findings support the idea that using citric acid to heal chronic wounds is beneficial and should be used in such cases.

Amol et al. (2012) investigated the effectiveness of citric acid in wound healing, particularly in the case of leg ulcers. Leg ulcers are very common in patients who already have chronic liver disease. They looked for the right person who had developed a leg ulcer. They discovered a forty-five-year-old man. He also had chronic liver problems as well as some unidentified issues. Leg ulcers in the past had been resistant to treatment of any kind. They applied three percent citric acid to the wound and left it there for a month. The wound was completely healed after a one-month treatment protocol. Citric acid is beneficial for ulcerative wounds, and it should be used to heal them, according to this recovery.

Mehdinezad et al. (2012) compared the wound-healing properties of zinc oxide and a *Verbascum Thapsus* extract. *Verbascum Thapsus* is said to be effective in the treatment of wounds. It improves the skin's resistance to invading microbes. It restores skin elasticity, allowing skin cells to fight invading germs. It brings back to life those cells that have died, restoring tissue functionality in the process. The reviewed article revealed that both zinc oxide and *Verbascum Thapsus* help to speed up the healing of skin wounds.

When recombinant human activated proetin type C was used to heal partial thickness burn wounds, Kritikos et al. (2012) observed activity. They compared it to antithrombin three and heparin to see how effective it was. They inflicted partial

thickness superficial wounds and deep partial wounds. For the study, they chose a porcine model. The research took place over the course of 48 hours. During this time, the elements in question were applied to wounds. All wound areas were subjected to histopathological examinations. Histopathology specimens were collected at various time intervals. In comparison to other agents, such as antithrombin three and heparin, the results of histopathological studies revealed that recombinant human activated proetin type C is superior. As a result, human activated proetin type C should be used to treat burn wounds.

Jalali et al. (2012) investigated the efficacy of *Achillea mille folium*, also known as yarrow, in the treatment of burn wounds. The yarrow plant is a traditional herbal remedy for treating burn wounds and sores. It has been used for thousands of years for this purpose. For the experiment, rabbits were chosen. A total of ten rabbits were chosen, all of which were healthy and free of any disease. They were split into two groups, each with five rabbits. The dorsal area of the rabbit's body was chosen for burn injuries. The wounds of group A were treated with normal saline wash only after the burn injuries were created, and they were kept as a control group. The yarrow extract was given to the remaining five rabbits in group B. The alcoholic extract of the yarrow plant was used to create this extract. The research took place over the course of twenty-one days. Microbiological examination, histopathology, wound contraction rate, and healing time were among the parameters investigated. On days seven, fourteen, and twenty-one, all of these parameters were investigated. According to the findings of the study, using the yarrow plant reduces wound contraction rate and healing time. Furthermore, it significantly reduces the wound's microbiological load, allowing it to heal more quickly. All of these evidences point to the yarrow plant's ability to aid in the healing of burn wounds.

Rezaie et al. (2012) investigated the effects of zinc oxide and *Matricaria* oil on skin

wound healing. Matricaria oil has been shown to be beneficial when used for healing purposes. Rats were chosen as the test animals. Rats' backsides were pierced with open wounds. These wounds were inadvertently inflicted. Zinc oxide is well-known for its absorptive and protective properties around the world. It's also thought to be a non-toxic metal oxide. Matricaria oil, on the other hand, is well known for its immune-boosting, anti-inflammatory, antimicrobial, and fibroblast activation properties. All of these factors play an important role in wound healing. The goal of this study was to see if zinc oxide or Matricaria oil was better at healing wounds. Seventy-five female rats were chosen to help us achieve our goal. They appeared to be in good health. They were assigned to one of five groups. There were fifteen rabbits in each group. The first group was designated as the control group, and their wounds were only washed with normal saline. The second group was treated as a placebo. The wounds of the third group were treated with a topical application of zinc oxide. Matricaria oil was given in high and low doses to groups four and five, respectively. Groups four and five received a ten percent Matricaria oil concentration, while group five received a twenty percent Matricaria oil concentration. The treatment was extended for another twenty-eight days. The biopsy samples were taken on days 0, 3, 7, 14, 21, and 28 after the surgical wounds were inflicted. In addition to histopathology, wound contraction rate and healing time were measured. The findings of the study revealed that ten percent Matricaria oil is far superior to zinc oxide in terms of wound healing, as it promotes faster wound healing and keeps the wound free of microbial growth. As a result, Matricaria oil is recommended for wound healing.

Cicco et al. (2014) investigated the effects of gentamicin sulphate in pectin nanoparticles. They created a gel with gentamicin sulphate embedded in pectin nanoparticles. They chose rabbits to conduct the experiment on. The study was carried out for a total of 21 days, with microbiological

examinations taking place on days 3, 7, 14, and 21. They tested the material's antibacterial and wound-healing properties. They discovered that GS had better antibacterial efficacy against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, as well as lower microbial load, than the control. They discovered that the moisture transmission of hydrogel was optimal for wound healing. Nano spray dried particles filled wounds with high encapsulation efficiency, good flowability, and proper adhesiveness. As a result, they discovered that proper drug dispersion and nanoparticle surface adhesion improved wound healing, and that drug delivery was a key to successful healing. They also discovered that GS combined with Pectin nano particles is more effective for wound healing than GS alone.

Lansdown et al. (2007) investigated the effect of zinc oxide in surgical wound treatment when combined with hydrocolloid dressing. The dressing was made by mixing zinc oxide with a hydrocolloid solution. They used a pig model to create forty surgically inflicted partial thickness skin wounds and treated them with zinc oxide hydrocolloid dressings. Wound closure, inflammation, and wound bacterial growth rates were among the evaluation parameters. They assessed all of these parameters for twenty-one days in a row. Only bacterial growth rate was inhibited, but there was no effect on wound closure or inflammation control, according to the findings. As a result, the study concluded that dressings were only beneficial for controlling microbial growth and had no effect on surgical wound healing, inflammatory response control, or wound contraction rate. As a result, its use is limited to bacterial growth control; therefore, it is recommended that it be used in conjunction with a wound healing agent to achieve the best results.

Sangeetha et al. (2011) used zinc nitrate and Aloe Vera leaves to check for Zinc Oxide nanoparticles. Their goal was to compare the effectiveness of this preparatory method to that of traditional methods such as physical and chemical methods. They achieved

a 95 percent conversion to nanoparticles by using a 25 percent concentration of Aloe vera leaves broth and Zinc nitrate. They used SEM and TEM methods to characterise nanoparticles. They discovered that nanoparticles ranged in size from 25 to 40 nm and were spherical after characterization. They also discovered that changing the concentration of aloe vera leaf broth can change the size of nanoparticles. As a result, this method is a good way to make Zinc oxide nanoparticles.

The antibacterial effect of zinc oxide nanoparticles was investigated by Yadollahi et al. (2014). Zinc oxide has been shown to have antibacterial properties, particularly against methicillin-resistant *Staphylococcus aureus*. This bacteria is particularly important in terms of wound contamination because it thrives there. Its management is critical to ensuring that wounds heal quickly. Because bacterial invasion at the wound site contributes significantly to the length of time it takes for a wound to heal. When zinc oxide is used in the form of nanoparticles, its antibacterial properties are thought to be enhanced. The purpose of this study was to confirm our hypothesis. Within carboxymethyl cellulose hydrogels, nanoparticles were created. X-ray diffraction, SEM, and UV-vis spectroscopy were used to characterise them. Nanoparticles ranged in size from 10 to 20 nano meters. The antibacterial properties of zinc oxide nanoparticle hydrogel were demonstrated using an agar diffusion test. This hydrogel was discovered to have antibacterial properties against *E.coli* and *Staphylococcus aureus*. As a result, it is beneficial in biomedical applications.

Janaki et al. (2015) investigated the effects of environmentally friendly zinc oxide nanoparticles. In the synthesis of nanoparticles, green technology eliminates all harmful protocols. Green technology was used to prepare nanoparticles using zinc carbonate and dried powder of ginger rhizome (*Zingiber officinal*). They used X-ray diffraction (XRD), scanning electron microscopy (SEM), and energy dispersive X-ray spectroscopy to

characterise them (EDX). To test the antibacterial activity of zinc oxide nanoparticles, four bacteria strains were used: *Klebsiellapneumoniae*, *Staphylococcus aureus*, *Candida albicans*, and *Penicilliumnotatum*. Antibacterial activity against these pathogens was confirmed using the well diffusion method. These nanoparticles were found to be very effective against these pathogens.

Tayel et al. (2010) compared the antibacterial properties of zinc oxide powder and zinc oxide nanoparticles. In this study, they used nine bacterial strains, the majority of which were foodborne. *Salmonella typhimurium* and *Staphylococcus aureus* were among the bacteria exposed to zinc oxide nanoparticles at minimal inhibitory concentrations. *Salmonella typhimurium* cell numbers were reduced to zero in 8 hours, and *Staphylococcus aureus* cell numbers were reduced to zero in 4 hours. According to the findings, zinc oxide nanoparticles are a more effective antibacterial agent than traditional zinc oxide powder in controlling bacterial growth.

Rath et al. (2015) used zinc oxide nanoparticles in a study to see if they could improve drug administration in post-surgical wounds. Cefazolinnano fiber mats were used to incorporate zinc oxide nanoparticles. Nanoparticles, it was hypothesised, have greater penetration power than standard zinc oxide, resulting in faster wound healing. Zinc oxide is already well-known for its anti-inflammatory and antibacterial properties, which help with wound healing. It also aids in the formation of new blood vessels. On the dorsal skin region of rats, surgical wounds were created. The wound healing properties of Cefazolin loaded with Zinc oxide nanoparticles were tested. Collagen synthesis was increased, and wound healing was hastened. *Staphylococcus aureus* was identified as the bacteria with the best inhibitory response. It is the most common bacteria that causes wound infection. Cefazolin mats containing Zinc oxide nanoparticles were used to effectively control it.

Rozaini et al. (2004) investigated the effect of honey on the healing of burned wounds. Honey is thought to be a good healer. When applied topically, honey is said to act as an antioxidant. It also prevents bacterial contamination of the wound. One of the most common causes of delayed wound healing is bacterial contamination. Furthermore, honey is safe to use because no cases of toxicity have been reported to date. Honey has different properties depending on the plants from which honey bees collect nectar. Recruiting was the first step in the study. There are a total of 155 male rats. All of the animals were in perfect health, with no signs of illness. Their backside was chosen for the purpose of creating burn wounds. A burn wound was created by heating cylindrical aluminium in a water bath. It was around a temperature of 80 degrees Celsius. Prior to inflicting burn injuries on animals, they were anaesthetized to ensure animal welfare. One group was treated with silver sulfadiazine cream as a control group. The other group received a topically applied honey treatment. This treatment was given for a total of twenty-one days. Tissue tensile strength, wound contraction rate, and healing time were all factors to consider. Rats were euthanized after 21 days of treatment, and the wound area was removed to test its tensile strength. This was accomplished using a universal testing machine. The honey-treated group's tensile strength was found to be higher than the control group's.

On full thickness cutaneous wounds in rats, Sazegar et al. (2011) tested the wound healing effects of zinc sulphate supplement alone and in combination with honey. They gathered a large sample size of 177 rats for their study. They were divided into four equal-sized groups. In order to ensure animal welfare, surgical wounds were created in all rats under general anaesthesia. Group one served as a control, while group two received zinc sulphate via oral administration. The third group was given honey as a topical treatment. For group four animals, a combination of oral zinc sulphate and honey application was used. The healing process continued until day 21.

Blood samples were taken from the animals on the 21st day to determine the concentration of zinc in their blood. Histological procedures necessitated the collection of tissue samples. Before tissue samples were taken, the experimental animals were euthanized. The tensile strength of healed tissue samples was tested. The rate of wound contraction was measured from the day the wound was inflicted until the 21st day, when healing was complete. Animals in groups 2, 3, and 4 showed a positive trend in wound healing, with tensile strength and histological examination results that sounded promising. In comparison to the control group, animals in groups 2, 3, and 4 showed a significant increase in collagen content, re-epithelization, and angiogenesis. Workers came to the conclusion that zinc sulphate in combination is a more effective wound healing agent than zinc sulphate alone.

Hajiaghaalipour et al. (2013) conducted a study to assess the wound-healing potential of *Camellia sinensis*, or tea. Tea has long been known for its skin-beneficial properties, as regular consumption keeps the skin healthy and glowing. *Camellia sinensis* leaves were used to make a methanolic extract. On the neck region of rats, full thickness cutaneous wounds were created. Twenty-four Sprague Dawley rats were used in the experiment. They were divided into four equal groups. On the neck region of rats, a 2cm excision skin wound was created. They were split into four different groups. The first group was given a 200gm/kg body weight methanolic extract of *Camellia sinensis*. The second group was given a 100gm/kg body weight methanolic extract of *Camellia sinensis*. The other two groups served as controls, receiving intrasite gel and 0.2 ml of vehicle Carboxy methyl cellulose (CMC) in normal saline 2 percent twice a day, respectively. Healing lasted for another ten days. On the tenth day, samples were taken for histopathological analysis. Less inflammatory changes were observed in wounds treated with *Camellia sinensis*, and scar tissue formation was also good. They also discovered that

wounds treated with *Camellia sinensis* have higher collagen content and angiogenesis. They came to the conclusion that *Camellia sinensis* has a lot of healing power.

Chong-Ming et al. (2007) conducted an experiment to demonstrate that when povidone iodine is mixed with sugar, it improves healing efficiency. They used female rats in the experiment and infected them with diabetes. Full-thickness skin wounds were created on the backs of these rats. A mixture of povidone iodine and sugar was used to treat the patients. When compared to the control group, epithelization was higher in the treated animals. The number of capillary lumens and granulation tissue were also counted in a complete wound cross section. It was discovered that combining sugar and honey povidone iodine speeds up wound healing and that it is also an effective treatment for diabetic wounds.

CONCLUSIONS

Wound healing is an intricate process in which after the injury the skin or other body tissues repair themselves, but some time healing can fail at any stage due to interruption. There are several factors which can delay the wound healing process, such as anaemia, diabetes, nutritional deficiency, hematoma, local infections, etc. In the treatment of wounds, many medicinal plants and other herbal immunomodulators such as honey, Neem leave, turmeric, *aloe vera*, etc, are considered useful. Zinc oxide nanoparticles and Zinc oxide wound healing is cheap, affordable, and healthy because it has no side effects. Via different pathways, these herbal ointments promote healing and regeneration of the lost tissues. There is, however, a need for scientific evaluation, standardization and safety assessment of these herbal ointments.

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